THE QUANTITATIVE SEPARATION OF QUININE AND STRYCHNINE.

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NO TWO DRUGS are more generally prescribed together than quinine and strychnine. They are found in such preparations as pills, syrups, tablets, powders, glycerites and elixirs. Owing to this fact their analysis becomes of importance to both the analyst and the toxicologist.

The dose of strychnine is very small, about one-sixtieth of a grain; the ordinary dose of quinine is comparatively large, two to five grains, the ratio of strychnine to quinine ranging from 1:30 to 1:120. It is this relatively small proportion of strychnine that renders the actual separation of these alkaloids one of the quite difficult problems confronting the pharmaceutical chemist.

Among the methods used by chemists to make this separation are: First, the ferrocyanide method; second, the oxalate method; and third, the tartrate method. The ferrocyanide method is based on the insolubility of strychnine ferrocyanide in strongly acid solution and the solubility of the quinine salt. The objection to the method is that the separation is not sharp. A small amount of quinine is carried down with the strychnine, giving a high apparent strychnine content.

The oxalate method is based on the relative insolubility of the oxalate of quinine and the solubility of the strychnine salt. The results by this method are generally too low for the strychnine content. Results 50 per cent lower than the actual strychnine content have been recorded.

The tartrate method, recommended by Vanderkleed, is carried out in a manner similar to the oxalate method. The quinine is precipitated as a tartrate and separated by filtration from the soluble strychnine tartrate. The tendency of this method is to give low results for strychnine.

Besides these gravimetric separation processes there are colorimetric methods for the determination of strychnine in the presence of quinine, among them being the color produced by strychnine in a sulphuric acid solution of potassium dichromate, and the color produced by oxidizing agents on

solutions of strychnine after treatment of the alkaloid with zinc and hydrochloric acid.

These methods are valuable as checks on gravimetric separation methods, but of course are of no value where a separation of the alkaloids is desired.

During the past few months I have been experimenting with a new method for the separation of these alkaloids, which in point of accuracy and simplicity seems to excel any method heretofore published. It is based on the comparative insolubility of strychnine chloroplatinate.

The chloroplatinate of strychnine is nearly insoluble in water, insoluble in alcohol, and practically insoluble in a mixture of alcohol 90 per cent and dilute hydrochloric acid 10 per cent. The chloroplatinate of quinine is soluble in water, fairly soluble in alcohol, and very readily soluble in the alcohol-hydrochloric acid mixture. It was from those facts that the following method was worked out.

Dissolve .050 grammes to .100 grammes of the mixed alkaloids (depending on amount of strychnine present) in a small amount of the alcohol-hydrochloric acid mixture (about 5 cc.) ; add 20 per cent solution of platinic chloride, drop by drop, while slightly agitating the mixture, until precipitation is complete. Add 5 cc. more of the solvent, cover with watch glass and set aside for one hour, then filter through tared filter, wash with alcohol, place in oven, dry at 100° C. for fifteen minutes, cool and weigh. If the proportion of quinine is large, it will be necessary to add 5 to 15 cc. more of the solvent before filtering. It will also be necessary to decompose the precipitate with alkali (NaOH), recover the strychnine with chloroform, evaporate and reprecipitate the chloroformic residue from a few cc. of the alcohol-hydrochloric acid solvent, with the platinic chloride reagent.

The chloroplatinate of strychnine is yellow in color, crystalline, and has a remarkable luster. It contains about 62 per cent of the alkaloid and 18 per cent of metallic platinum.

The chloroplatinate of quinine has an orange color and an amorphous appearance.

A trace of chloroplatinate of quinine gives an amorphous appearance to the chloroplatinate of strychnine—a valuable indication of the purity of the strychnine salt.

The amount of strychnine can be calculated from the weight

of the chloroplatinate, from the amount of metallic platinum, or directly by the decomposition of the chloroplatinate.

By this method it has been found possible to determine the strychnine in a mixture of .060 of quinine and .002 of strychnine, being about the proportions found in such preparations as elixir of iron, quinine and strychnine.

In determining the strychnine in the elixir of iron, quinine and strychnine, it would be necessary to liberate the total alkaloids and proceed with the mixed alkaloids as directed. The quinine can be determined by difference or from the filtrate by making alkaline, shaking out with ether or chloroform, and weighing the dried residue.

The only interfering alkaloid in this separation is brucine. Brucine, if present, would behave similarly to strychnine. Dionin, morphine, narcotine, codeine, heroin, atropine, colchicine, hydrastinine, narceine, coniine, cocaine, aconitine, scopolamine, physostigmine, pilocarpine, theobromine, cinchonine, antipyrine and caffeine are not precipitated from their acid alcoholic solutions. It is the rule, however, that most alkaloids are precipitated from their *alcoholic* solutions. The exceptions are dionin, atropine, colchicine, narceine, coniine, aconitine, theobromine, antipyrine, and caffeine. Dionin, colchicine, coniine, theobromine and caffeine are not precipitated from any of their solutions by the platinic chloride reagent.